REMARKS

This Response Under 37 CFR §1.115 is respectfully submitted in response to the Office Action rendered April 16, 2007. This Response is timely in view of the concurrently filed Petition for Extension of Time. Claims 15-22 are pending and Claims 1-14, 17 and 23-29 are canceled. Claims 30-34 have been added. They find basis in the Specification at p. 7, l. 1-14, *inter alia*.

The Office Action of April 16, 2007 again rejected Claim 22 under 35 U.S.C. §102(a) as being as anticipated by Kelly et al. (WO 99/36050) ("Kelly"). Applicants respectfully request reconsideration of this rejection in view of the ensuing discussion.

The Office Action indicates that Kelly et al. teach "that the ratio of organic solvent…in water may be as low as 0.1%" in the extraction process set forth therein [Office Action, p. 3]. The Office Action argues that such a low ratio of ethanol would be unlikely to denature proteins therein. Applicants respectfully submit that this observation is conjectural and request reconsideration in view of the ensuing discussion.

Applicants respectfully submit that the Kelly reference describes *ingestible* fractions of soybean that *do not* contain trypsin inhibitory activity. In connection with the method of extracting isoflavones from soybeans, the Kelly et al. reference alludes to a previously-published application that describes a method of preparing the isoflavone compounds that are described therein, WO93/23069 (hereinafter, "the '069 publication"):

> Extracts of soy or clover may be prepared according to WO93/23069, the teachings of which are incorporated by reference. *As described in WO98/23069 soy or clover may be extracted with a mixture of organic solvent* (such as ethanol, chloroform, acetone, ethyl acetate and the like) and water. The ratio of solvent in water may be from 0.1% to 99.9%, preferably 40% to 60%. [WO99/36050, p. 11, l. 23-27] (emphasis added)

The '069 publication describes the extraction method in Example 1, at p. 18, l. 4-17, as follows:

> The dried material is extracted in an aqueous: organic solvent mix. The aqueous phase is required to extract the water-soluble glycoside form of isoflavones, while *the organic solvent is required to solubilise the water-insoluable aglycone form.* The organic solvent can be either alcohol, chloroform, acetone or ethyl acetate. The ratio of solvent in the water can be between 0.1% and 99.9%. *The preferred method is to use 60% alcohol in water.*
>
> The isoflavones are extracted by exposing the plant material to the water:solvent mix. *The exposure time in general terms is indirectly proportional to the temperature of the mixture*. The temperature of the mix can range between ambient temperature and boiling temperature. The exposure time can be between 1 hour and 4 weeks or even longer. *It has been determined that the adequate times for maximal recovery of isoflavones are 2 weeks at 50°C and 24 hours at 90°C.* The supernatant is separated from the undissolved plant material and the organic solvent removed by distillation. ['069 Publication, p. 18, l. 4-17] (emphasis added)

Applicants also respectfully note that the compositions described in the '069 Publication were intended for oral consumption:

> This invention relates to natural products containing phyto-oestrogens, or phyto-oestrogen metabolites, which have various beneficial physiological effects in man, and which have a variety of uses, such as to promote good health and *as a dietary additive*, for example. [WO93/23069, p. 1. l. 1-3] (emphasis added)

Thus, the phyto-estrogen or isoflavone products described in WO93/23069 were *required* to be fit for oral consumption by humans. In order to meet this requirement, any possible proteins present in the Kelly isoflavone products must have been denatured so as *not* to contain soy trypsin inhibitor proteins—these proteins would cause gastrointestinal illness. Thus, whether or not the products set forth in the Kelly et al. publication and WO93/23069 have similar activity to those of the compositions and methods of applicants' invention, they *cannot* constitute the same soy fraction and could not have contained active trypsin inhibitor proteins. The conclusion that two extracts are identical merely because they have similar activity is unsubstantiated: there are many separately patentable paths to achieve the same result. Similarly, applicants have surprisingly found that a soybean extract containing trypsin inhibitory activity can achieve the claimed

results. The Kelly reference does not describe or suggest utilizing a soybean extract for the claimed methods of use containing proteins that have trypsin inhibitory activity.

Applicants therefore respectfully submit that the soy extract set forth in Kelly is *not* non-denatured and the recitation of a "non-denatured" soy product is not inherent in Kelly as the Office Actions asserts. Applicants therefore respectfully request reconsideration of the foregoing rejection.

The Office Action of April 16, 2007 again rejected Claims 15-16, 18-21, and 30 under 35 U.S.C. 103(a) as being unpatentable over Tokuyama (JP 5-320061), in view of Mizue (JP 62-36304). The Office states as follows:

> Tokuyama teach using aqueous or organic extract of soy beans and/or other legumes in unaltered form in topical dermatological compositions for treating a variety of skin diseases and conditions such as scratches, cuts, burns, rashes, eruptions, pimples, blackheads, chapping skin, eczema, dermatitis, etc….Moreover, the soy bean extracts applied to the skin as cosmetic products showed 'a smoothing effect on the texture of the skin,' 'a wrinkle stretching rejuvenating effect,' 'skin softening and moisturizing effect,' and 'an aging preventing effect'…" [Office Action, p. 4]

The Office Action also mentions that "even though product-by-process claims are limited by and defined by the process; determination of patentability is based on the product itself." [Office Action, p. 5] Further, the Office Action states that "Mizue teach stabilizing soy extracts in cosmetic compositions with preservatives such as parabens and chelating agents such as disodium EDTA…" [Office Action, p. 6]

Applicants respectfully request reconsideration of this rejection in view of the ensuing discussion.

Applicants respectfully submit that the products set forth in Tokuyama are different from those claimed in instant application. Tokuyama did not recognize the importance of maintaining the STI activity and is not concerned that the extract retains serine protease inhibitory activity. Tokuyama describes the extracted activity as "unknown component [which] is stable in the presence of heat" (p.3), whereas STI, which provides activity in the claimed invention, is known to be heat labile. (See previously-submitted Declaration of Miri Seiberg, ¶5)

Moreover, Tokuyama uses high temperatures "in extraction by boiling…" (Tokuyama, p.3) and other extraction procedures such as extreme pH or organic solvents

(..."pretreatment with an acid or alkali"... (p.4), ..."processed in organic solvent extraction"), all of which processes are known to denature proteins, thereby eliminating STI's protease inhibitory activity. Thus, applicants respectfully submit that Tokuyama neither describes nor suggests the compositions and methods of applicants' invention.

Nor does Mizue compensate for the inadequacies of Tokuyama in directing those of ordinary skill in the art toward applicants' claimed invention. The Office Action relied on Mizue to teach stabilizing soy extracts in cosmetic compositions with preservatives such as parabens and chelating agents such as disodium EDTA. [Office Action, p. 5] The Office Action than concluded that it would have been obvious to one having ordinary skill in the art at the time of the invention was made to modify the cosmetic or dermatological soy extract-containing compositions of Tokuyama to add chemical agents such as preservatives.

Applicants respectfully submit that Mizue, taken together with Tokuyama or separately, would not render the compositions and methods of applicants' invention obvious. Although Mizue discusses means for preserving soy extracts present in a composition, it does not provide means for obtaining the non-denatured, active STI-containing extracts of the compositions of applicants' invention. Rather, Mizue teaches stabilization in terms of *prevention* of degradation or decomposition. Mitzue does not describe or teach stabilization of *proteins*, which could be intact but *inactive* upon denaturation. There is no teaching in Mizue that the addition of a paraben (which is a microbicide) or a chelaotr such as EDTA (which prevents oxidation by metal ions through complexation with ambient metal ions) would protect the activity of *proteins*.

Thus, neither Tokuyama nor Mizue describes or suggests compositions containing *active proteins*.

The Office Action notes that:

> …even though product-by-process claims are limited by and defined by the process; determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." [Office Action, p. 5].

In response, applicants respectfully submit that the claims are drawn to a method of using a particular type of soybean extract that is not suggested or described by the

prior art. Applicants respectfully point out that the term "nondenatured" is an adjective describing the nature of the active materials of the compositions and methods of their invention rather than a limitation to a process of producing. "Nondenatured" as used in applicants' Specification describes a soy material that contains active soy trypsin inhibitor proteins. Applicants further respectfully submit that a mere similarity in activity should not render a method of treatment unpatentable. There are most certainly differences in the properties of denatured and nondenatured soy materials: denatured soy has had its proteins rendered inactive. The mere fact that two different fractions or extracts of soy have activity on the skin does not establish that utilizing one would have rendered obvious the use of another.

In view of the foregoing discussion, applicants respectfully request reconsideration of the rejections set forth in the Office Action of April 16, 2007. An early allowance is earnestly solicited. Kindly direct any questions or contacts to the undersigned.

Respectfully submitted,

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